

10/506630

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/US03/06910

## A. CLASSIFICATION OF SUBJECT MATTER

IPC(7) : C12N 9/00; C12P 19/62  
 US CL : 435/183, 76

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)  
 U.S. : 435/183, 76

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)  
 CAPlus

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	MCDANIEL et al. Engineered intermodular and intramodular polyketide synthase fusions. Chemistry & Biology. September 1997, Vol. 4, pages 667-674, especially Figure 4 plasmid KAO318.	1-4, 6-8, 11, 12
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Y		9, 10, 13-15, 27, 29-31
X	RANGANATHAN et al. Knowledge-based design of bimodular and trimodular polyketide synthases based on domain and module swaps: a route to simple statin analogues. Chemistry & Biology. October 1999, Vol. 6, pages 731-741 especially Figure 3 plasmid TKS-AR2.	16, 21, 23, 24
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Y		27, 29
Y	US 5,712,146 A (KHOSLA et al.) 27 January 1998 (27.01.1998), columns 2, 4, and 13-14.	9, 10, 13-15, 27, 29-31

☐ Further documents are listed in the continuation of Box C.

☐ See patent family annex.

## \* Special categories of cited documents:

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier application or patent published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" documents published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art

"&" document member of the same patent family

Date of the actual completion of the international search

04 November 2004 (04.11.2004)

Date of mailing of the international search report

20 DEC 2004

Name and mailing address of the ISA/US

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## Box I Observations where certain claims were found unsearchable (Continuation of Item 1 of first sheet)

This international report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claim Nos.:  
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☒ Claim Nos.: 5, 18-20, 22, 25 and 26  
because they relate to parts of the international application that do not comply with the prescribed requirements to such an extent that no meaningful international search can be carried out, specifically:  
Please See Continuation Sheet
3. ☐ Claim Nos.:  
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

## Box II Observations where unity of invention is lacking (Continuation of Item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:  
Please See Continuation Sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this international search report covers all searchable claims.
  2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
  3. ☐ As only some of the required additional search fees were timely paid by the applicant, this international search report covers only those claims for which fees were paid, specifically claims Nos.:
  4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this international search report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:
- Remark on Protest ☐ The additional search fees were accompanied by the applicant's protest.  
☐ No protest accompanied the payment of additional search fees.

# INTERNATIONAL SEARCH REPORT

PCT/US03/06940

## Continuation of Box I Reason 2:

Claims 5 and 20 do not comply with the prescribed requirements to such an extent that no meaningful search could be carried out because Claims 5 and 20 are wholly unclear. Claim 5 depends from Claim 1, which requires naturally occurring extender modules (not hybrid modules) be used; extender modules minimally comprise three domains known as KS-AT-ACP, in that order. However, in Claim 5, the claim requires a "hybrid" extender module wherein KS and AT are from one PKS and ACP is from a different PKS. Thus, the intent of the claim is wholly unclear and, thus, cannot be meaningfully searched. The same reasoning for Claim 20 is applied since Claim 20 also requires a naturally occurring extender module be used.

Claims 18, 19, 22, 25, and 26 do not comply with the prescribed requirements to such an extent that no meaningful search could be carried out because Claims 18, 19, 22, 25, and 26 are wholly unclear. Claim 16, from which all the instant claims depend, requires that the first naturally occurring extender module and the second naturally occurring extender module by "not normally downstream" which can only be interpreted as not of the same PKS. However, each of Claims 18, 19, 22, 25, and 26 require the first and second modules to be of the same PKS (or both of the ery PKS). Thus, the intent of the claims is wholly unclear and, thus, cannot be meaningfully searched.

## BOX II. OBSERVATIONS WHERE UNITY OF INVENTION IS LACKING

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1. In order for all inventions to be examined, the appropriate additional examination fees must be paid.

Group I, claim(s) 1, 3, 4, 6-16, 21, 23, and 24, drawn to methods of making a hybrid modular polyketide synthase (PKS) and hybrid PKSs.

Group II, claim(s) 2 and 17, drawn to methods of making polyketides using a hybrid PKS.

Group III, claim(s) 27 and 29-32, drawn to methods of making a hybrid nonribosomal peptide synthetase-modular polyketide synthase (NRPS-PKS) and hybrid NRPS-PKSs.

Group IV, claim(s) 28, drawn to methods of making polyketides using a hybrid NRPS-PKS.

The inventions listed as Groups I-IV do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons. The methods in Group I share a special technical feature of making particular hybrid polyketide synthase enzymes using naturally occurring PKS extender modules, intrapolypeptide linkers and interpolypeptide linkers in particular method steps; this special technical feature includes both the starting materials and the product in the method steps. The methods of Groups II and IV do not share this special technical feature with Group I because the products of the claimed methods in Groups II and IV are not in common with the special technical feature of Group I since the polyketide products (small organic molecules) of Groups II and IV are different from the hybrid polyketide synthase enzyme products of Group I. The method of Group III also does not share the special technical feature of Group I because neither the products nor the starting materials are in common with those of Group I with the inclusion of NRPS modules in the hybrid PKS produced in Group III.